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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Bibb *et al.*

Application No.: 09/687,959

Group Art Unit: 1632

Filed: October 13, 2000

Examiner: Shukla, Ram R.

For: METHODS OF IDENTIFYING AGENTS THAT REGULATE PHOSPHORYLATION / DEPHOSPHORYLATION IN DOPAMINE SIGNALING

Old Attorney Docket No: 600-1-257 CIP
New Attorney Docket No.: 11181-013

Confirmation No.: 8464

TRANSMITTAL OF DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants submit herewith a Declaration of Allen A. Fienberg, Ph.D. Under 37 C.F.R. § 1.132. The Declaration is submitted further in response to the Office Action dated March 29, 2002 (Paper No. 10, "Office Action"), issued in connection with the above-identified application. In the Office Action, the Examiner rejected pending claims 16-21 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification as filed, particularly contending that the specification is not enabling for the claimed invention because there is no evidence of record to indicate that an agent that inhibits DARPP-32 at Threonine-75 ("Thr75-DARPP-32") would treat any disease and neither the specification nor the art of record teaches how a skilled artisan would practice the claimed methods without undue experimentation (Office Action, page 3).

The Declaration is submitted to explain that a skilled artisan could routinely use the teachings of the specification coupled with the state of the art at the time of the claimed priority date to routinely make and use the claimed invention, and that, as taught in the specification, the *in vitro* biochemical results and *in vivo* results showing treatment of a dopamine dysregulation disease can be correlated. This correlation is demonstrated in the

specification in which a compound identified via the *in vitro* methods is demonstrated to treat a dopamine dysregulation disease in an art-accepted animal model for such a disease. In view of the evidence presented by way of the Declaration submitted herewith, Applicants respectfully request that the rejection of claims 16-21 under 35 U.S.C. § 112, first paragraph be withdrawn.

Applicants believe that no fee is due in connection with the filing of this transmittal. However, should the Patent Office determine otherwise, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Entry of the foregoing remarks is respectfully requested.

Respectfully submitted,

Date: September 30, 2002

Nikolaos C George 39,201
Nikolaos C. George (Reg. No.)

By: Anne M Schneiderman 43,095
Anne M. Schneiderman (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosure

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Bibb *et al.*

Application No.: 09/687,959 Group Art Unit: 1632

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Old Attorney Docket No: 600-1-257 CIP
New Attorney Docket No.: 11181-013

Confirmation No.: 8464

DECLARATION OF ALLEN A. FIENBERG, PH.D.
UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, ALLEN A. FIENBERG, Ph.D., do declare that:

1. I am the Vice President of Business Development at Intra-Cellular Therapies, Inc., the exclusive licensee of the above-identified patent application. A copy of my curriculum vitae is attached as Exhibit 1.

2. I have read and understood the above-identified patent application and the Office Action dated March 29, 2002, issued in connection therewith.

3. I understand that the above-identified application is a continuation-in-part application of prior Application No. 09/419,379, filed October 15, 1999 (now abandoned). I understand that the claimed priority date is October 15, 1999.

4. I understand that at page 3 of the Office Action, the Examiner has rejected pending claims 16-21 as allegedly not enabled by the specification as filed, particularly contending that the specification is not enabling for the claimed invention because there is no evidence of record to indicate that an agent that inhibits DARPP-32 at Threonine-75 ("Thr75-DARPP-32") would treat any disease and neither the specification nor the art of record teaches how a skilled artisan would practice the claimed methods without undue experimentation. The Examiner thus rests his rejection on an alleged lack of correlation between an agent that inhibits phosphorylation of Thr75-DARPP-32 and the use of that agent to treat a dopamine dysregulation disease.

5. I am making this declaration to explain that the biochemical effect of inhibition of phosphorylation of Thr75-DARPP-32 does indeed correlate with the ability to treat a dopamine dysregulation disease. In particular, as discussed hereinbelow, the *in vitro* methods taught in the specification for identification of compounds for use in the methods of the invention, *e.g.*, Cdk5 modulators, do work, as taught, to identify such compounds, and that furthermore, the use of the art-accepted animal model of a dopamine dysregulation disease taught in the specification demonstrates and verifies that the *in vitro* methods indeed work. Briefly, as discussed in detail hereinbelow, there is indeed a correlation between the *in vitro* biochemical results described in the specification and *in vivo* results, using the model, showing treatment of a dopamine dysregulation disease. This correlation is demonstrated in the specification (at Example 2, pages 61-67), in which a compound identified via the *in vitro* methods, roscovitine, is demonstrated to treat a dopamine dysregulation disease in an art-accepted rat model for such a disease.

The Specification Provides Sufficient Guidance for Identification of Agents for Use in the Meth ds of the Invention and for Using the Agents in the Methods of the Invention

6. In certain embodiments, the invention provides a method for treating dopamine dysregulation in a patient comprising administering to the patient an agent that either inhibits the phosphorylation of Thr75-DARPP-32 or promotes the dephosphorylation of Thr75-DARPP-32. In particular, certain embodiments of the invention are drawn to a method for treating dopamine dysregulation in a patient comprising administering to the patient an agent that inhibits the phosphorylation of Thr75-DARPP-32 by Cdk5. As detailed below, as of the claimed priority date of the application, the skilled artisan, armed with the teachings of the specification and with what was routinely known in the art at that time, could have (a) identified compounds that modulate, *e.g.*, inhibit, the phosphorylation of Thr75-DARPP-32, *e.g.*, by Cdk5, and (b) these compounds could routinely be tested *in vivo* and be shown to, indeed, treat a dopamine dysregulation disease, as was demonstrated in the specification in Example 2.

7. The specification teaches, at pages 28-30, at Example 1 (pages 57-60) and at Example 2 (pages 61-67), *in vitro* and *in vivo* methods for identifying compounds that modulate the phosphorylation of Thr75-DARPP-32. The specification teaches that such compounds can be used to treat a dopamine dysregulation disease (at Example 2, pages 61-67). Further, the specification demonstrates that a compound, roscovitine, identified by the methods of the invention, modulates the phosphorylation of Thr75-DARPP-32. In particular, roscovitine is shown to be effective in treating a dopamine dysregulation disease in an art-accepted model for such a disease.

The Animal M del Taught in the Specification Was an Art-Accepted Model for a Dopamine Dysregulation Disease

8. The specification teaches that *in vivo* animal models can be used to corroborate that compounds identified by the *in vitro* methods taught in the specification can be used to treat a dopamine dysregulation disease. In particular, the specification teaches (at page 29, line 12 to page 30, line 16) that alternatively, or in conjunction with *in vitro* assays, an animal model can be used to ascertain the effect of a potential agent on a dopamine-related condition and that a potential modulator that ameliorates the dopamine-related condition can then be selected. It would have been recognized by the skilled artisan, from the teachings in the specification, that an animal model can thus be used to corroborate the results of the *in vitro* brain slice assay as taught in the specification, and to corroborate the effect of a potential agent on a dopamine dysregulation disease.

9. For example, in Example 2, the specification teaches the use of an art-accepted rat model for a dopamine dysregulation disease (*i.e.*, drug addiction, psychosis and/or schizophrenia induced by chronic intake, *i.e.*, daily administration, of cocaine) in which the activity of dopaminergic intracellular signaling pathways can be analyzed (*see* Example 2, pages 61-67). This art-accepted rat model for a dopamine dysregulation disease, in which the rat received five daily injections of cocaine (15 mg/kg, i.p.), was used to corroborate that, as also observed in the *in vitro* brain slice assay taught at Example 1 (pages 57-60), bilateral intra-accumbens infusion of roscovitine, a selective Cdk5 inhibitor, markedly potentiated activity of dopaminergic pathways. Roscovitine potentiated the rat's locomotor activity and augmented cocaine's effects on locomotor activity over successive days of injection (page 64, line 26 to page 65, line 15). Infusion of a less selective Cdk5

inhibitor, olomoucine, also potentiated cocaine's locomotor effects (page 65, lines 4-11). As taught in the specification at page 65, line 16 to page 67, line 22, inhibition of Cdk5 by a selective inhibitor, *e.g.*, roscovitine, enhances sensitization to repeated doses of cocaine and exacerbates cocaine-induced locomotor activity. As taught at page 18, lines 22-25 of the specification, roscovitine increases locomotor behavior in rats, which is the predicted effect of inhibition of Cdk5 phosphorylation of Thr75 of DARPP-32, thus demonstrating the potential of Cdk5 inhibitors to modulate dopamine dysregulation.

10. As of the claimed priority date, the animal model taught in the specification, the rat model for a dopamine dysregulation disease (induced by chronic intake of cocaine), was widely accepted and used in the art. Furthermore, as of the claimed priority date, rat models for a dopamine dysregulation condition, *e.g.*, drug addiction, psychosis and/or schizophrenia, were commonly known in the art to entail injecting subjects daily with cocaine (see, *e.g.* Hiroi *et al.*, 1999, Neuronal and behavioral abnormalities in striatal function in DARPP-32 mutant mice, European Journal of Neuroscience 11: 1114-1118, Ref. DB of record; Shimosato *et al.*, 1995, Increased polyamine levels and changes in the sensitivity to convulsions during chronic treatment with cocaine in mice, Brain Research 684: 243-247, Ref. DE of record; Masserano *et al.*, 1994, Effects of chronic cocaine administration on ^{3}H-dopamine uptake in the nucleus accumbens, striatum and frontal cortex of rats, J. Pharmacol. Exp Ther. 270: 133-141, Ref. DC of record; which are each submitted concurrently herewith in a Second Supplemental Information Disclosure Statement).

11. Such rodent models for a dopamine dysregulation disease were viewed in the art as providing insights into the neurobiological bases of human dopamine-related

diseases or conditions, *e.g.*, drug addiction, psychosis and/or schizophrenia. For example, as of the claimed priority date, the reinforcing effects in rodent models of indirect sympathomimetics, *e.g.*, cocaine and amphetamine, were known by skilled artisans to depend on release of dopamine in the terminal fields of the mesocorticolimbic dopamine system, and the acute reinforcing effects of opiates in rodent models were known to involve the activation of dopamine (*see, e.g.*, Koob and Nestler, 1997, The neurobiology of drug addiction. J. Neuropsychiatry Clin. Neurosci. 9(3):482-97, Ref. DF of record, submitted concurrently herewith in a Second Supplemental Information Disclosure Statement). Activation of the mesolimbic dopamine system was known to trigger relapse in a rat model of cocaine-seeking behavior, and this activation was known to be selectively induced by D2-like, and not by D1-like, dopamine receptor agonists. In a rat model of cocaine addiction, D1-like receptor agonists had been observed to prevent cocaine-seeking behavior induced by cocaine itself, whereas D2-like receptor agonists had been observed to enhance this behavior (*see* Self *et al.*, 1996, Science 271(5255):1586-89, Opposite modulation of cocaine-seeking behavior by D1- and D2-like dopamine receptor agonists, Ref. DD of record, submitted concurrently herewith in a Second Supplemental Information Disclosure Statement). These results were viewed as a demonstration of the dissociation between D1- and D2-like receptor processes in cocaine-seeking behavior and to support further evaluation of D1-like receptor agonists as a possible pharmacotherapy for cocaine addiction (*see* Self *et al.* at pages 1586 and 1588).

12. Hence, using the teachings of the specification, the skilled artisan could have used techniques well known in the art to identify agents that modulate the phosphorylation of Thr75-DARPP-32. A skilled artisan would have viewed the rat model for a dopamine dysregulation disease, as taught in the specification, as an acceptable animal

model in which to test the effects of these agents on treatment of a dopamine dysregulation disease. Furthermore, contrary to the Examiner's allegations at page 5 of the Office Action, a skilled artisan would recognize that the results of Figure 9 of the specification, which shows the effect of Cdk5 inhibitors (roscovitine and olomoucine) on the locomotor behavioral response of the rat, could be extrapolated to a human patient, and that administration of the Cdk5 inhibitors increased the activity of dopaminergic pathways (*i.e.*, prolonged the cocaine-induced increases in locomotor behavior).

13. Thus, as taught in the specification, use of an art-accepted animal model for a dopamine dysregulation disease was used to corroborate that a selective Cdk5 inhibitor, roscovitine, potentiated the activity of dopaminergic intracellular signaling pathways. Such an inhibitor would have been recognized by the skilled artisan, as of the claimed priority date, as being useful in the treatment of a dopamine dysregulation disease, *e.g.*, Parkinson's disease, wherein activity of dopaminergic pathways is reduced, and wherein potentiation of the activity of dopaminergic intracellular signaling pathways leads to amelioration of symptoms of the disease.

The *In Vitro* Brain Slice Assay Taught in the Specification Was an Art-Accepted Assay That Correlates With Results Observed *In Vivo*

14. In addition, as of the claimed priority date, results from the *in vitro* methods taught in specification were accepted by skilled artisans to correlate with results from *in vivo* animal models. The experimental assay taught in the specification (at Example 1, pages 57-60) for analyzing the activity of dopaminergic intracellular signaling pathways, the *in vitro* mouse brain slice assay, was widely accepted in the art. The mouse brain slice

assay was recognized by skilled artisans as an *in vitro* model for wild-type brain structure and function (see, *e.g.*, Hemmings *et al.*, 1989, J. Biol. Chem. 264: 7726-33, Ref. AU of record; Girault *et al.*, J. Biol. Chem. 264: 21748-59, Ref. AO of record; Fienberg *et al.*, Science 281: 838-42, Ref. CW of record; PCT publication WO 99/20273 by Nishi *et al.*, published April 29, 1999, Ref. CZ of record, submitted concurrently herewith in a Second Supplemental Information Disclosure Statement, "Nishi I"; and U.S. Patent No. 6,013,621, by Nishi *et al.*, issued January 11, 2000, Ref. CY of record, submitted concurrently herewith in a Second Supplemental Information Disclosure Statement, "Nishi II," incorporated by reference in its entirety in the specification, see page 18, lines 1-2). As of the priority date of the application, the brain slice used in the assays discussed in the paragraphs hereinabove was accepted by skilled artisans as a physiologically functional sample of brain tissue. Such brain slices (*e.g.*, striatal slices) were recognized as being composed of the full complement of heterogenous cells that make up the brain structure from which the slice is excised. It was routinely known that many of the cells in the slice preparation maintain their *in vivo* patterns of connectivity with other cells in the slice, as well as their *in vivo* physiological function, including the expression of intracellular signaling molecules, *e.g.*, G proteins, protein phosphatases, protein kinases, etc. Using the brain slice model, the skilled artisan could therefore have routinely assayed for neuronal connectivity and function using standard histological, biochemical and electrophysiological methods, and used the results of the assay to predict connectivity and function *in vivo*.

15. As of the claimed priority date, moreover, the *in vitro* mouse brain slice assay was accepted by skilled artisans as having predictive value in determining whether administration of a potential agent had ameliorative effects on a dopamine dysregulation

disease. For example, the specification discloses (at page 29, lines 12-18) that the methods of U.S. Patent No. 5,777,195 (issued July 7, 1998 to Fienberg *et al.*, Ref. CW of record) may be used to select a potential modulator that ameliorates a dopamine-related condition. U.S. Patent No. 5,777,195, of which I am a co-inventor, discloses an *in vitro* assay using striatal brain slice slices from wild-type and DARPP-32 knockout mice, which is used to determine the effects of administration of agents that target different parts of a dopaminergic pathway than that disclosed in the present specification (*e.g.*, D1 receptor, sodium-potassium ATPase) and that ultimately result in different biochemical effects than inhibition of Thr75-DARPP-32 phosphorylation. U.S. Patent No. 5,777,195 discloses that the *in vitro* assay can be used to determine the effects of dopamine or D1 agonists (*e.g.*, the compound APB) on the inhibition of calcium channel currents, on the inhibition of the activity of sodium-potassium ATPase, and on striatal neuron excitability such as firing threshold (col. 13, lines 27-64). U.S. Patent No. 5,777,195 discloses that the mouse brain slice assay can be used to analyze the physiological responses of striatal neurons to administration of amphetamines (col. 13, lines 27-64, citing the methods of Surmeier *et al.*,1995, Neuron 14(2):385-97, Ref. CK of record). U.S. Patent No. 5,777,195 also discloses that the mouse brain slice assay may be used in conjunction with an *in vivo* assay of locomotor activity in animals administered a drug of abuse (cocaine) to analyze the role of DARPP-32 in intracellular signaling pathways by which the drug of abuse acts in an animal (col. 13, line 65 to col. 14, line 9). Such coupling of an *in vitro* mouse brain slice assay with an *in vivo* mouse locomotor assay was accepted by skilled artisans, as of the claimed priority date, as an experimental approach that is directly predictive of the potential ameliorative effects of an agent of interest on dopaminergic dysregulation in a human patient (*see also*, Nishi I (Ref. CZ of record) and Nishi II (Ref. CY of record)).

16. Furthermore, as of the claimed priority date, it was well within the skill of a skilled artisan to select a potential agent whose effects in humans were previously unknown and to determine whether it could be used to inhibit Thr75-DARPP-32 phosphorylation and to treat a dopamine dysregulation disease. As discussed in the paragraphs hereinabove, it was routine in the art, for example, to test a potential agent in a mouse striatal brain slice assay. Subsequent testing of the effect of the potential agent on behavior, *e.g.*, locomotor behavior, in a rat model of dopamine dysregulation could have been routinely accomplished and based on the outcomes of one or both of these assays, as taught by the specification, the potential agent's effects on the amelioration of dopamine dysregulation could have been predicted. Using the methods taught in the specification, a skilled artisan would have been enabled to routinely identify other compounds useful for practicing the methods of the invention, *e.g.*, other members of the indirubin or paullone families, which would have been expected to be useful in treating a dopamine dysregulation disease as taught in the specification (see Office Action at page 5).

17. As of the claimed priority date, it was also well within the skill of a skilled artisan to select dosage regimens for testing in clinical trials, based on the experimental results obtained from animal models, and subsequently, to select a dosage regimen based on the results of the clinical trial. For example, Masserano *et al.* discloses that animal models for human schizophrenia are based on the observation that chronic intake of amphetamines or cocaine by humans can produce clinical symptoms similar to symptoms of schizophrenia (page 133, col. 1). Masserano *et al.* also discloses that animal models for human "amphetamine psychosis" induced by chronic intake of amphetamines or cocaine have been developed based on the observation that the repeated administration of amphetamine or

cocaine to rats can produce a behavioral sensitization in these animals, and can be measured by an enhanced locomotor or stereotypic response when these rats are subsequently challenged with these stimulant drugs (page 133, cols. 1-2). Masserano *et al.* also discloses a rat model for schizophrenia based on the abstinence syndrome seen in chronic human cocaine abusers (pages 133-139) that may serve as an animal model for the cocaine abstinence syndrome in humans and discloses uptake studies of [^{3}H]-dopamine into cells of the nucleus accumbens, striatum and frontal cortex after chronic treatment of the rats with cocaine. Masserano *et al.* draws correlations between the data obtained in rats and that observed in human cocaine abusers (page 139, col. 2 to page 140, col. 1). It concludes, based on both the data from the rat model and from the data from the human cocaine abusers (which included cocaine binding studies in the brain observed through positron emission tomographic (PET) scanning) that the frontal cortex plays a role in the symptomatology of schizophrenia seen in human cocaine addicts and schizophrenics (page 139, col. 2 to page 140, col. 1).

18. It should be noted, moreover, that the specification teaches the use of an agent that modulates a dopaminergic intracellular signaling pathway by inhibiting the phosphorylation of Thr75-DARPP-32 or promoting the dephosphorylation of Thr75-DARPP-32 (page 10, lines 11-15). As of the claimed priority date, knowing that a particular agent of interest specifically modulated only a dopaminergic intracellular signaling pathway (*e.g.*, a D1- and/or D2-receptor mediated pathway), and not other intracellular signaling pathways, would not have been necessary to practice the claimed invention throughout its scope, nor would such specificity have been viewed by a skilled artisan as requisite for practicing the methods of the invention (see Office Action at page 5). I emphasize that as of the claimed priority date, skilled artisans recognized that the modulation of DARPP-32 phosphorylati n

would necessarily modulate the activity of a dopaminergic intracellular signaling pathway, whether or not it also modulated other signal transduction pathways, *e.g.*, NMDA, AMP, GAB VIP, 5HT4 or A2A intracellular signaling pathways. Armed with such knowledge, a skilled artisan could have practiced the claimed methods of the invention and, indeed, determined whether "the effect [of a potential agent would] be there in vivo" (Office Action at page 5) and whether administration of the agent would produce an ameliorative effect in a patient.

19. Thus, as discussed hereinabove, the specification actually demonstrates the correlation of results obtained in an *in vitro* brain slice model with those obtained in an *in vivo* rat model. Furthermore, as of the claimed priority date, the state of the art was such that the rat model disclosed in the specification at Example 2 (pages 61-67) was recognized as correlating to a dopamine dysregulation disease, *e.g.*, drug addiction, psychosis and/or schizophrenia. The use of an *in vitro* animal model (mouse brain slice assay), coupled with an *in vivo* animal model (rat model for cocaine addiction) was accepted in the art to have predictive value in determining whether administration of a potential agent will produce ameliorative effects on dopamine dysregulation or on a dopamine dysregulation disease (see also specification at page 29, line 12 to page 30, line 16). Using the methods taught in the specification, coupled with the knowledge available in the art for conducting and analyzing assays in the *in vitro* brain slice and *in vivo* model (*i.e.*, the rat model for a dopamine dysregulation disease), the skilled artisan would be enabled to determine, without undue experimentation, whether a potential agent identified by the methods taught in the specification could be used to treat a dopamine dysregulation condition.

20. As discussed hereinabove, the teachings of th specification would have enabled the skilled artisan, armed with routine knowledge, as taught in the referenc s above, to practice the methods of the invention without undue experimentation, hence rebutting the rejection, at pages 3-7 of the March 29, 2002 Office Action, that the claimed invention is not enabled because, as of the claimed priority date, one skilled in the art would not have been able to practice the claimed method of treatment without undue experimentation.

21. I declare further that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 9/30/02

ALLEN A. FIENBERG, PH.D.

Attachment:

Exhibit 1: Biographical Sketch - Allen A. Fienberg

BIOGRAPHICAL SKETCH – ALLEN A. FIENBERG

NAME	POSITION TITLE
ALLEN A. FIENBERG	PRINCIPAL INVESTIGATOR

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
University of California, Berkeley, CA	B.A.	1981	Genetics
Yale University, New Haven, CT	Ph.D.	1991	Human Genetics

A. POSITIONS AND HONORS.

JAN. 2002-PRESENT	FOUNDER & VICE PRESIDENT OF BUSINESS DEVELOPMENT, ITI, NEW YORK, NY
JUN. 2001-DEC. 2002	THE ROCKEFELLER UNIV., ASSISTANT PROFESSOR FOR RESEARCH
1999-2001	THE NOVARTIS INSTITUTE FOR FUNCTIONAL GENOMICS, LA JOLLA, CALIFORNIA, STAFF SCIENTIST THE ROCKEFELLER UNIV., GUEST INVESTIGATOR
1993-1999	THE ROCKEFELLER UNIV., RESEARCH ASSOC., ADVISOR: P. GREENGARD, PH.D., LAB. OF MOL. AND CELLULAR NEUROSCIENCE
1991-1993	THE ROCKEFELLER UNIV., POSTDOCTORAL ASSOC., ADVISOR: P. GREENGARD, PH.D., LAB. OF MOL. AND CELLULAR NEUROSCIENCE
1984-1991	YALE UNIVERSITY, GRADUATE RESEARCH, ADVISOR: DR. FRANK RUDDLE, PH.D., DEPT.OF BIO. AND HUMAN GENETICS
1982-1984	UNIVERSITY OF CALIFORNIA, BERKELEY, RESEARCH ASSOC., DEPT. OF GENETICS
1978-1981	UNIVERSITY OF CALIFORNIA, BERKELEY, UNDERGRAD. RESEARCH, DEPT. OF GENETICS
AWARDS:	1984-1988 LUCILLE P. MARKEY SCHOLAR

B. SELECTED PEER-REVIEWED PUBLICATIONS (IN CHRONOLOGICAL ORDER).

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RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

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